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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/994,909	11/23/2001	George Jackowski	2132.090	7376

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 05/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/994,909	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 39-46* is/are pending in the application.

4a) Of the above claim(s) *39-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

ttachment(s)

) ☐ Notice of References Cited (PTO-892)

) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/15/3*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claim 1 has been amended, claims 2-38 have been cancelled and claims 39-46 have been added as requested in the amendment of Paper filed on March 12, 2004. Claims 1 and 39-46 are pending in the instant application.

2. Newly submitted claims 39-46 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 39-43 are directed to methods of diagnosing Alzheimer's disease, classified in class 435, subclass 4, for examples; and claims 44-46 are directed to a diagnostic kit, classified in class 530, subclass 387.1, for example. Invention of claim 1 and the invention of claims 39-43 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the newly presented claims are directed to methods that do not use the claimed protein itself, only information obtained therefrom. Inventions of claim 1 and claims 44-46 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the peptide of claim 1 and kit comprising antibodies of claims 44-46 are distinct inventions because peptides and antibodies are physically and functionally distinct chemical entities, and because the protein can be used in another and entirely different process from the use for production of

the antibody, such as in a pharmaceutical composition in its own right, or to assay or purify the natural ligand of the protein.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 39-46 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim 1 is under examination in the instant office action.

3. Applicant's argument of the decision *In re Ochiai* (pages 10-11 of the Response) is noted but is not deemed persuasive, as PTO practice in view of that decision is directed to rejoinder of claims after allowable subject matter has been indicated, and not to withdrawal of restriction requirements. Applicant is advised that at such time as elected product claim(s) are indicated as being allowable, claims directed to the using such allowable product will also be examined. Applicant's request for rejoining the claims directed to methods of using the allowable product is acknowledged.

4. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

6. Applicant's arguments filed on March 12, 2004 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112

7. Claim 1, as amended, stands rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for those reasons of record in section 4 of Paper No. 13. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Applicant's reference to MPEP 2165.03 (top at page 17 of the Response) appears to be misplaced because MPEP 2165.03 relates to the requirements for Rejection for Lack of Best Mode wherein the instant rejection pertains to the lack of enablement of the claimed invention.

Applicant further traverses the instant rejection on the premises that "electrophoretic, mass spectrometric and chromatographic techniques are well-known to those of skill in the art, thus [...] one of skill in the art would be familiar with the techniques used and would know how to carry out the protocols in the instant disclosure" (bottom at page 17 of the Response). The Examiner fully agrees with this statement. However, the issue at hand remains not the ability of one to "carry out the protocol" but the ability of one to follow the protocol and practice the invention with a reasonable expectation of success. The skill in the art is high and it is obvious that no undue experimentation would be required for a skilled artisan to follow any of the electrophoretic or mass spectrometry protocols presented in the instant specification. However, because the assertion of association of the instant peptides with Alzheimer's disease is not supported by any evidence of record, a skilled artisan would have to resort to substantial undue experimentation to discover how to use the claimed peptides for diagnostic purposes. The

Examiner maintains the position, which was fully explained in the previous office action, that the instant specification, as filed, fails to provide any evidence or sound scientific reasoning that would support a conclusion that the isolated peptides consisting of amino acid residues 2-14 of SEQ ID NO: 1 could be used in diagnosis for Alzheimer's disease.

Applicant argues that analysis and comparison of the lanes shown in Figure 1 between serum samples of Alzheimer's disease patients and normal control demonstrates that "band C2 can be said to be down-regulated in Alzheimer's disease" (middle at page 19 of the Response). Applicant provides explanation of Figure 1, which in summary reflects that bands C1, C2 and C3 are differentially expressed in samples obtained from AD patients and age-matched control samples ("[b]ands C1 and C3 appear as strongly expressed as compared with band C2 of corresponding location in different lanes"). Isolation of the claimed peptide of SEQ ID NO: 1 from all three bands is asserted to support the conclusion that "[s]ince this protein appears to be down-regulated in Alzheimer's disease, it is considered to be indicative of Alzheimer's disease" (page 19). Thus, according to the information provided in the instant specification, as filed, and additionally in Applicant's response, all samples contain the claimed biopolymer marker of SEQ ID NO: 1, fragment 2-14. However, it is obvious that in order for a peptide to be indicative of a disease, a marker diagnostic for Alzheimer's disease, the peptide must be either present or absent or differentially expressed in Alzheimer's disease sample *versus* normal sample. If it is a "down-regulation" of the claimed peptide that is indicative of Alzheimer's disease, then a particular critical information regarding the level of expression of the claimed peptide, for example, must be provided. The Examiner maintains the position that the instant specification fails to provide any guidance on how to use the claimed biopolymer marker peptide consisting of amino acid

residues 2-14 of SEQ ID NO: 1 for diagnosis of Alzheimer's disease because it clearly lacks a disclosure of a method of evaluation of the samples, thus requiring undue experimentation on part of a skilled artisan in order to be able to use the instant claimed peptide as a marker for Alzheimer's disease.

The Declaration of Jackowski under 37 CFR 1.132 filed on March 12, 2004 is insufficient to overcome the rejection of claim 1 for the following reasons. The Declaration presents more detailed explanation on how to analyze the data obtained by the protocol disclosed in the instant specification. In particular, it states that "[t]he bands, which differ between healthy and diseased patients diseased patients, are excised and purified from the gel. A determination of up-regulation, down-regulation, presence and/or absence of the proteins present in the bands is assessed by sample wherein they appear, for example, the claimed peptide fragment was identified and excised from a band which appeared to be weakly expressed in the diseased samples as compared to the age-matched samples" (section 4 of the Declaration). Thus, it appears that the Declaration provides more clarification on how a peptide of SEQ ID NO: 1 was discovered to be present in serum samples of AD patients rather than enables to use the claimed peptide for diagnosis of AD. For example, if an unknown sample presented for analysis and the sample contains a fragment 2-14 of SEQ ID NO: 1, does this indicate the presence or absence of Alzheimer's disease? Moreover, according to Applicant's arguments that the method of analysis of the samples "requires identification of differences in the spectra of the disease state versus the spectra of the non-disease state. Such simple analysis does not require "undue experimentation"" (middle at page 21 of the Response), it appears that in order to use the instant claimed peptides for diagnosis of Alzheimer's disease, samples must be already identified as normal or diseased

samples, after which "[t]he relationship is observed from a comparison of disease spectra to normal (healthy) spectra". One skilled in the art readily recognizes that diagnosis of a disease assumes first finding of a distinguishing symptom, such as a specific marker in a sample, which leads to identification of a specific pathological condition.

Furthermore, even if to assume that the claimed peptide could be used for diagnosis of Alzheimer's disease, the series of questions regarding the description of the samples used for analysis remains unanswered. The instant specification, as filed, fails to present any description of the samples used in experiments to determine the presence or absence of the claimed marker. There is also no information presented regarding up- or down-regulation of the instant peptide 2-14 of SEQ ID NO: 1 in serum samples of pathological conditions other than Alzheimer's disease, or serum samples of patients suspected of having Alzheimer's disease, in which such marker would be present, followed up by a diagnosis of AD by using other diagnostic methods. A skilled practitioner readily recognizes that in the absence of such critical information Applicant's invention is incomplete, which leads to a substantial amount of undue experimentation to discover how to use the claimed biopolymer marker consisting of amino acids 2-14 of SEQ ID NO: 1 in diagnosis of Alzheimer's disease with no assurance of success.

Applicant submits that the references provided in the previous office action, which clearly state that a definitive diagnosis of Alzheimer's disease could be only made during postmortem examination or at brain biopsy, are more than five years old and, therefore, "these references are not considered to accurately assess the state of the art at the time of the Applicant's invention" (page 21-22 of the Response). This argument has been fully considered but is not deemed persuasive because the presented references still represent the state of the art in

the field of diagnosis of Alzheimer's disease. If Applicant is aware of any art, which was available prior to the filing date of the instant application, which describes any method of definitive diagnosis of Alzheimer's disease by methods other than by direct brain tissue analysis, then Applicant is strongly encouraged to make such art of record.

Thus, in view of the lack of teachings found in the prior art or presented in the instant disclosure as set forth earlier, and also the total absence of the working examples, the instant specification is not found to be enabling for use of peptide 2-14 of SEQ ID NO: 1 for diagnosis of Alzheimer's disease. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use Applicants' invention as currently claimed.

Conclusion

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.

OLGA N. CHERNYSHEV, PH.D.
PATENT EXAMINER